Safety Data Sheet

Diphenylamine

Division of Safety
National Institutes
of Health

WARNING!

THIS COMPOUND IS TOXIC AND POSSIBLY TERATOGENIC. IT IS ABSORBED THROUGH THE SKIN AND RESPIRATORY AND INTESTINAL TRACTS. AVOID FORMATION AND BREATHING OF AEROSOLS OR VAPORS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND COLD WATER. AVOID RUBBING OF SKIN OR INCREASING ITS TEMPERATURE.

DPA IS FLAMMABLE. KEEP AWAY FROM SPARKS AND OPEN FLAMES. IN CASE OF FIRE, USE CARBON DIOXIDE OR DRY CHEMICAL EXTINGUISHER.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, DRINK MILK OR WATER. REFER FOR GASTRIC LAVAGE. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. AVOID SKIN CONTACT OR BREATHING OF AEROSOLS OR VAPORS. USE ETHANOL TO DISSOLVE COMPOUND. USE ABSORBENT PAPER TO MOP UP SPILL. WASH DOWN AREA WITH SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

A. Background

Diphenylamine (DPA) is a white crystalline compound with a floral odor, practically insoluble in water but soluble in most organic solvents. It is absorbed by inhalation (as dust) and by skin and eye contact. It is used in industry as an intermediate in dye manufacture, antioxidant, propellant stabilizer, antiwear additive to lubricants, and in photoimaging. Agricultural uses include

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topical formulations in anti-screwworm mixtures and in various devices to prevent storage scald in apples and other fruit. In the analytical laboratory DPA is a reagent for the detection of nitrate, chlorate, and other oxidants, and in the determination of deoxyribose in purine or (with modification) pyrimidine nucleotides ("Dische reaction") (Dische, 1955; Blakley, 1966). DPA is moderately toxic by oral administration and possibly teratogenic in rats.[A] Carcinogenicity or mutagenicity has not been demonstrated.

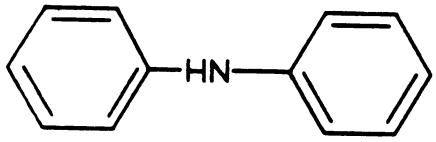
There is no federal standard for exposure to DPA. ACGIH (1987) recommends a TWA of 10 mg/m^3 of dust. A Russian publication sets the maximum permissible level in reservoir waters at 0.05 mg/l (Korolev et al., 1976).

B. Chemical and Physical Data

1. Chemical Abstract No.: 122-39-4.

2. Synonyms: N-phenylaniline; anilino benzene; benzenamine, N-phenyl[B]; C.I. 10355; DFA; DPA. Trade names: Big Dipper; No Scald; Scaldip.

3. Chemical structure and molecular weight:



$C_{12}H_{11}N$; 169.24.

4. Density: d_4^{25} = 1.16; vapor density = 5.82.

5. Absorption spectroscopy: Ultraviolet absorption maximum at 284 nm (Reynaud and Rumpf, 1963). Mass spectral data have been published (Eland and Danby, 1965).

6. Volatility: Vapor pressure data over the range of 1 mm - 760 mm Hg are listed on p. D-216 in Weast (1982).

7. Solubility: DPA is practically insoluble in water. One gram dissolves in 2.2 ml ethanol and 4.5 ml propanol. Freely soluble in benzene, ether, glacial acetic acid, carbon disulfide.

8. Description: White crystals (monoclinic leaves from ethanol). Floral odor. DPA is a very weak base (pK_a = 0.86, Reynaud and Stumpf, 1963) whose salts are decomposed by water.

9. Boiling point: 302°C; melting point: 54°C.

See note at beginning of F.
Chemical Abstracts name, used for listing in 9th Decennial Index and ubsequently.

10. Stability: DPA appears to be stable under ambient conditions the dark. On exposure to light discoloration occurs. Heating to 1000°C at low pressure produces carbazole as major pyrolysi product (Wentrup and Gaugaz, 1971).

11. Chemical reactivity: DPA undergoes the usual substitution reactions at the phenyl rings of most aryl compounds. The H atom of the imino group is replaceable by alkali metals. DPA alkylated in the para positions by isobutylene, styrene, etc. and in the ortho positions by olefins. Dehydrogenation produc carbazole. Reacts rapidly with oxidants.

12. Flash point: 153°C (closed cup).

13. Autoignition temperature: 634°C.

14. Explosive limits in air: No data.

Fire, Explosion and Reactivity Hazard Data[A]

1. Use carbon dioxide or dry chemicals as fire extinguishants. While the fire hazard due to heat or flame exposure is small, inhalation or skin exposure to DPA dust should be avoided. Therefore fire-fighting personnel should wear air-supplied respirators with full face masks.

2. DPA is incompatible with strongly oxidizing materials.

3. Hazardous decomposition products are highly toxic fumes of NO_x.

4. Do not expose to sparks and open flames. Use non-spark tools and equipment.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The NIH Guidelines should be consulted to identify the proper use condition required and specific controls to be implemented during normal and complex operations or manipulations involving DPA.

It should be emphasized that this data sheet and the NIH Guidelines are intended as starting points for the implementation of good laboratory practices when using this compound. The practices and procedures described in the following sections pertain to the National Institutes of Health and may not be universally applicable

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[A]Information based on Sax, 1984.

to other institutions. Administrators and/or researchers at other institutions should modify the following items as needed to reflec their individual management system and current occupational and environmental regulations.

1. Chemical inactivation: No validated method reported.

2. Decontamination: Turn off equipment that could be affected by DPA or the materials used for cleanup. If there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 116) for assistance. Use absorbent paper to mop up spill. Wipe off surfaces with ethanol, then wash with copious quantities of water. Glassware should be rinsed (in a hood) with ethanol, followed by soap and water. Animal cages should be washed wit water.

3. Disposal: No waste streams containing DPA shall be disposed o in sinks or general refuse. Surplus DPA or chemical waste streams contaminated with DPA shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., anima carcasses and bedding) containing DPA shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing DPA shall be disinfected by heat using a standard autoclave treatment and package for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with DPA shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactiv waste containing DPA shall be handled in accordance with the NI radioactive waste disposal system.

4. Storage: Store solid DPA and its solutions in dark-colored, tightly closed containers, preferably under refrigeration. Avoid exposure to light and moisture. Store working quantities of DPA and its solutions in an explosion-safe refrigerator in the work area.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

There is practically no information on this subject. A gas chromatographic procedure for the routine screening of water source for trace organic contaminants has been described (Burchill et al., 1983). A mobile mass spectrometer system has been used for the determination of aniline, benzothiazole, and DPA in urban air (Lane et al., 1980).

Biological Effects (Animal and Man)

Note: The information given below on absorption, metabolism, and acute toxicity can in all likelihood be ascribed to DPA itself. As far as toxic effects are concerned, such as development of renal cystic disease, it has been found that they may be due mainly if no entirely to a small amount of a contaminant in commercial DPA (Crocker et al., 1972) which has been identified as N,N,N'-triphenyl-p-phenylene diamine (Clegg et al., 1981) along with other contaminants. This impurity is not detected in standard tests for purity such as chromatography, and is visualized only upon deliberate overloading of chromatograms. It is removed only by ver vigorous recrystallization procedures. Prolonged heating of commercial or purified DPA (e.g., 195°C for 12 hours) produces this contaminant in larger amounts. From a practical point of view, it should be emphasized that industrial use of, and therefore potentia exposure to, DPA involves material which has not been so purified. The same caveat may well be relevant to the teratogenic findings described below.

1. Absorption: A review (Sittig, 1981) mentions that DPA may be introduced into the animal organism by inhalation of dust, skin absorption, and eye contact. No detailed studies of this aspec have been found. Experimentally, DPA is administered to animal orally (either as an admixture to the diet or in alcoholic solu tion by stomach tube), or by intraperitoneal injection.

2. Distribution: No data.

3. Metabolism and excretion: There appers to be considerable variation according to species and/or route of administration (Alexander et al., 1964, 1965) but, in general, the variation consists of differing loci of oxidation. In the rat (intra-peritoneal administration) the major urinary metabolite is the glucuronide of 4-hydroxy DPA, with minor amounts of 4,4'-di-hydroxy DPA glucuronide with no free DPA, 2-hydroxy DPA, or N-hydroxy DPA. In the rabbit (oral dosage) the urinary excretion products are mainly the glucuronide and sulfate of 4-hydroxy DPA with small amounts of unconjugated 4-hydroxy DPA, 2-hydroxy DPA, and unmetabolized DPA. In man, a single oral dose of DPA resulted in excretion of DPA, 4-hydroxy DPA, and 4,4'-dihydroxy DPA, mostly if not entirely in unconjugated form. While there is no direct evidence of oxidation at the nitrogen atom in any species (a metabolic step for many other aromatic amines) it is perhaps significant that oral administration of DPA, but not of N-acetyl DPA, resulted in a considerable metho-globinemia. In addition to urinary excretion of DPA in various metabolic forms, there is also significant excretion in the bile.

4. Toxic effects: The acute oral LD50 for rat, mouse, and guinea pig has been reported to be in the range of 2,000-3,000, 1,750,

and 300 mg DPA per kg, respectively. When 0.5 LD50 was administered to rats there was a decrease in hemoglobin and oxyhemoglobin content of the blood and the appearance of methemoglobin; all these blood indexes had reverted to normal between 10-14 days after administration (Volodchenko, 1975).

Prolonged feeding of DPA to rats results in nephrotoxicity. There is first a defect in the urinary concentrating ability and morphological changes in collecting tubules, followed by dilation of these tubules, necrosis, and formation of cysts composed of necrotic cells. In the terminal stages, the kidney resembles the adult type of human polycystic kidney disease (Kime et al., 1962; Thomas et al., 1967a; Safouh et al., 1970; Evan et al., 1978). The same effects are produced in the offspring of rats after feeding DPA to their mothers during the last days of gestation (Crocker et al., 1972). In the dog no nephrotoxicity has been noted but instead a moderate degree of liver function impairment with mild fatty degeneration (Thomas et al., 1967b). No other species seems to have been studied.

5. Carcinogenic effects: None has been reported, though the only pertinent study involved a single oral dose of DPA and observation for six months (Griswold et al., 1966).

6. Mutagenic and teratogenic effects: DPA is not mutagenic in the Ames test (Ferretti et al., 1977; Florin et al., 1980) and in tests for gene mutation in a mouse lymphoma assay (Amacher et al., 1980). The effects in newborn rats following DPA administration to pregnant mothers, which may indicate teratogenicity, have been mentioned above.

Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. Skin should not be rinsed with organic solvents. Since DPA is readily absorbed through the skin, avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes. Obtain ophthalmological evaluation.

2. Ingestion: Drink plenty of water or milk. Refer for gastric lavage.

3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

4. Refer to physician at once. Consider treatment for pulmonary irritation.

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